REMARKS

I. Status Summary

Claims 1-43 are pending in the present application. Claims 1-43 currently stand rejected by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Claims 28 and 29 have been objected to.

Claims 1, 28, and 29 have been amended. New claims 44 and 45 have been provided. Support for the amendments and new claims can be found in the application as filed. No new matter has been added. Therefore, upon entry of Amendment A, claims 1-45 will be pending in the subject application.

Reconsideration of the application as amended and further in view of the remarks set forth hereinbelow is respectfully requested.

II. Claim Objections

Claims 28 and 29 have been objected to. In particular, the Patent Office has noted that it appears that claims 28 and 29 do not end in a period.

Applicants thank the Patent Office for the observation concerning claims 28 and 29, and respectfully submit that claims 28 and 29 have been amended by the addition of a concluding period (i.e., "."). Accordingly, applicants respectfully believe that the Patent Office's objections have been addressed. Applicants further believe that claims 28 and 29 are in condition for allowance and respectfully request a Notice of Allowance to that effect.

III. Response to the Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1-43 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement because the claims are alleged to contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the claimed subject matter. In particular, the Patent Office alleges that the quantity of experimentation necessary to practice the full scope of the invention is great, "with little if any reasonable expectation of success." See Office Action, middle of page 3.

Further, the Patent Office alleges that the specification, while providing general guidance as to how assays may be conducted, fails to disclose specific starting materials or reaction conditions that would enable the full scope of the claimed subject matter. See Office Action, bottom paragraph of page 3. The Patent Office alleges that the specification does not set forth reaction conditions and starting materials where any metal oxide is used, where any solid support is used, or how any ligand-binding pair can be used in combination with the claimed method. See Office Action, middle of page 4.

The Patent Office notes that in claim 1, a capture probe is provided that hybridizes to the target nucleic acid and appears to be a nucleic acid. The Patent Office further notes that claim 14 recites an oligonucleotide detection probe. The Patent Office contends that if oligonucleotide is added in claim 14, there can be no oligonucleotide probe in claim 1, and that, therefore, it is unclear how hybridization is taking place. See Office Action, bottom paragraph of page 4.

The Patent Office similarly notes that claim 6 recites a probe comprising a nanoparticle and one member of a binding pair. The Patent Office alleges that if binding between the probe and the target is through the binding pair, it does not seem possible for any hybridization to take place in claim 1. See Office Action, top paragraph of page 5.

The Patent Office contends that both prior and post-filing art teaches numerous problems confronting those of ordinary skill in the art that have not been addressed by the instant disclosure, and particularly notes that the presently claimed method places no lower limit on the ability to accurately and reproducibly detect any binding between "polymer and unit specific markers." Thus, the Patent Office contends that the instant disclosure fails to identify art-recognized issues such that the full scope of the invention can be practiced without the public having to resort to undue experimentation. See Office Action, page 9.

The Patent Office contends that the claimed method encompasses the use of any hybridization conditions, any surface, nanoparticles of any size, shape and composition, and the use of any wavelength of light that could be absorbed by the

nanoparticle. Thus, the Patent Office alleges that present claims fairly encompass the detection of any nucleic acid, which is not required to be free of other materials, including partially complementary sequences, and wherein target and/or probe sequences can form secondary structures, leading to the observation of false positive signals. See Office Action, paragraph bridging pages 9 and 10.

Finally, the Patent Office contends that the arguments provided in Amendment A, filed on December 22, 2006, relate to what one of skill in the art would have been able to do or would have concluded after reading the instant disclosure. The Patent Office, referring to Manual of Patent Examining Procedure (hereinafter "MPEP") § 2145, contends attorney argument is not evidence unless it is an admission and that the arguments of counsel cannot take the place of evidence in the record.

After careful consideration of the rejection and the Patent Office's comments, applicants respectfully traverse the rejection and offer the following remarks.

Initially, applicants respectfully submit that with regard to whether the enablement is commensurate with the scope of the claims, "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." See MPEP § 2164.08, citing *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The scope of enablement must only bear a "reasonable correlation" to the scope of the claims. Id., citing *In re Fisher* 427, F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1070). In particular, "how a teaching is set forth, by specific example or broad terminology, is not important." Id., citing *In re Marzocchi*, 439, F.2d 220, 223-24 169 USPQ 367, 370 (CCPA 1971); emphasis added. Further, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled so long as a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. See MPEP § 2164.08(b), citing *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). That some experimentation may be necessary, and may be complex, does not make it undue if it is no more complex than that typically engaged in the art. See MPEP §

2164.01. See also, *In re Certain Limited-Charge Cell Culture Microcarriers*, 221, USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub. nom., Massachusetts Institute of Technology v. A. B. Fortia*, 774 F. 2d 1104, 227 USPQ 428 (Fed. Cir. 1985) and *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

Without acquiescing to the rejection, applicants respectfully submit that claim 1 has been amended herein to recite that the nanoparticle comprises an approximately spherical metal-atom entity having a diameter of less than 1000 nanometers and that exhibits one of surface plasmon resonance and an interband transition. Support for this amendment can be found in the instant specification at page 28, lines 32-33, which recites that a nanoparticle is an approximately spherical metal atom-comprising entity, and at page 29, lines 4-5, which recites that nanoparticles are generally less than 1000 nm in diameter. Support can also be found in the instant specification at page 29, lines 16-20, which recites that the nanoparticle can comprise a material that exhibits surface plasmon resonance, and in the instant specification at page 29, lines 22-23, which recites that the nanoparticle material can exhibit interband transitions. Additional support can be found in the instant specification at page 11, lines 29-31, which recites that the nanoparticle "absorbs light at one or more particular frequencies (e.g. exhibits surface plasmon resonance or integrand transition)".

Claim 1 has further been amended to recite that the wavelength of light to which the solid surface is exposed is absorbed by the nanoparticle and not by the solid surface. Support for this amendment can be found in the instant specification at page 22, lines 13-15, which recites that "the solid substrate can be any material that does not absorb significantly at the light excitation wavelength used for nanoparticle irradiation."

Claim 1 has also been amended to recite that the capture probe comprises at least one oligonucleotide sequence that specifically hybridizes to the target nucleic acid sequence under stringent hybridization conditions. Support for the amendment can be found in the instant specification at page 21, lines 15-18, which recites that each probe comprises at least one oligonucleotide sequence which is complementary

to a nucleic acid sequence of a target sequence, such that the oligonucleotide sequence (i.e., referring to the probe oligonucleotide sequence) "specifically hybridizes to the target sequence under stringent conditions."

Applicants respectfully disagree with the Patent Office's comments concerning the lack of specific starting materials or reaction conditions to enable the full scope of the claims. Applicants respectfully submit that the instant specification provides a great deal of guidance, both specifically and more broadly, regarding these matters. In particular, with respect to nanoparticles, the instant specification at page 28, lines 31-33, recites that "typically, but not necessarily, a nanoparticle is an approximately spherical metal atom-comprising entity." The instant specification recites various representative size ranges for nanoparticles at page 29, lines 4-13, as well as various metals and metal oxide nanoparticle materials at page 30, lines 4-10, including metal oxides such as iron (III) oxide, tin oxide, titanium dioxide, indium tin oxide (ITO), and ruthenium oxide. Fabrication methods and commercial sources for nanoparticles are recited in the instant specification at page 30, line 23 to page 31, line 9. The instant specification also describes metal nanoshell nanoparticles at page 31, line 10 to page 32, line 22.

The instant specification recites that the nanoparticle can comprise a material that is able to absorb light (see Instant Specification, page 11, line 29), and that absorbance causes the nanoparticle to generate heat. See Instant Specification, page 3, lines 25-26. The instant specification recites that the wavelength can match the surface plasmon resonance of the nanoparticle material (see Instant Specification, page 12, lines 13-14, and page 41, lines 5-7) or match another wavelength absorbed by the nanoparticle, such as the wavelength at which the nanoparticle metal component undergoes interband transition. See Instant Specification, page 29, lines 22-23, and page 41, lines 7-10. In particular, the instant specification recites that "the skilled artisan will be able to readily determine whether a putative nanoparticle material exhibits surface plasmon resonance" in view of what is known in the art or based on a determination made using methods known in the art. See Instant Specification, page 29, lines 17-20. The instant specification further

recites wavelength ranges for gold, silver and metal oxide nanoparticles (see Instant Specification, page 41, lines 19-25). Claims 30 and 31 as filed also each recite a particular nanoparticle material (i.e., gold or silver) and a specific light wavelength or wavelength range to be used. In laboratory examples described in the instant specification, the thermographic detection of gold nanoparticles is performed using light excitation at a wavelength of 532 nm. See, for example, Instant Specification, page 60, lines 3-7, and lines 17-23. See also, Instant Specification, Figures 10 and 11.

With regard to solid surfaces, the instant specification recites, as described hereinabove, that the solid substrate (i.e., the solid surface) can be any material that does not absorb significantly at the light excitation wavelength used for nanoparticle irradiation. See Instant Specification, page 22, lines 13-15. The instant specification further recites a number of specific materials from which the solid substrate can be constructed. See Instant Specification, page 22, lines 21-26 and page 22, line 33 to page 23, line 5. Example 3 describes thermography experiments involving the irradiation of gold nanoparticles on ITO substrates (see Instant Specification, page 60, lines 3-8 and lines 17-21) and on glass substrates (i.e., glass slides). See Instant Specification, page 60, lines 21-29. See also, Instant Specification, Figures 10 and 11.

Numerous functional groups and attachment chemistries are described for attaching oligonucleotides to other surfaces. See, for example, Instant Specification, page 25, line 15 to page 27, line 12. More specifically, the instant specification notes that phosphorothioate groups can be used to bind oligonucleotides to gold, while aminosilanes and alkylsiloxanes can be used to bind oligonucleotides to silica and glass. See Instant Specification, page 27, lines 1-10. Further, in describing the attachment of oligonucleotides to nanoparticles (see Instant Specification, page 32, line 25 to page 35, line 24), phosphonates and amines are recited for use in attaching oligonucleotides to metal oxides. See Instant Specification, page 34, line 27 to page 35, line 1. Example 1 specifically describes attaching a DNA sequence to

an indium tin oxide (ITO) surface. See Instant Specification, page 57, line 32 to page 58, line 17. See also, Instant Specification, Figure 4.

The instant specification recites that target sequences can be between ten and 50 nucleotides in length, but can also be shorter or longer. See Instant Specification, page 16, lines 13-20. In particular, the instant specification recites that the target sequence can be 300 nucleotides long or even longer. See Instant Specification, page 16, lines 19-20.

The instant specification describes various isolation and extraction methods related to nucleic acids. See, for example, Instant Specification, page 16, line 30 to page 17, line 21; and at page 18, lines 1-8. The instant specification recites that amplification of the target nucleic acid can be desirable in some cases (see Instant Specification, page 18, lines 21-23), but that the use of a sandwich assay can eliminate or reduce the need for such amplification. See Instant Specification, page 18, lines 17-20. Amplification methods are described in the instant specification at page 18, line 23 to page 19, line 22.

The instant specification describes that probes (e.g., capture or detection probes) can be oligonucleotide sequences of from 5 to 50 nucleotides or of from 50 to about 200-300 nucleotides or longer. See Instant Specification, page 21, lines 19-24. The specification further recites that the probes comprise an oligonucleotide sequence which "specifically hybridizes to the target sequence under stringent conditions." See Instant Specification, page 21, lines 15-18. In particular, Example 1, describes the use of complementary 18 base pair single-stranded DNA sequences attached to an ITO solid surface and a gold nanoparticle (i.e., an 18 nucleotide target sequence attached to the nanoparticle and an 18 nucleotide capture probe attached to ITO). See Instant Specification, page 58, lines 18-20.

The instant specification describes stringent hybridization conditions at page 38, lines 5-16, specifically reciting that under stringent conditions "a probe hybridizes specifically to its target sequence, but to no other sequences." Representative stringent hybridization conditions for nucleotides having more than 100 complementary residues are recited in the instant specification at page 38, lines 22-

32, while those for sequences of 10 to 50 nucleotides are described at page 39, lines 1-4. Further the instant specification describes specific higher stringency conditions, and notes that conditions can be generally rendered more stringent by the addition of formamide. See Instant Specification, page 39, lines 5-15.

With regard to the Patent Office's comments concerning claim 14, applicants respectfully submit the instant specification describes embodiments involving sandwich format hybridization assays in which a series of hybridization reactions can be performed. See Instant Specification, page 35, lines 27-30, emphasis added. Such an assay can comprise, for example, providing a capture probe attached to a solid surface and having a sequence complementary to a first domain of a target sequence. See Instant Specification, page 36, lines 12-14. The target sequence is contacted with the capture probe under conditions suitable for hybridization. See Instant Specification, page 36, lines 14-16. The solid surface with the capture probe-target sequence hybridization complex (i.e., the first hybridization complex) is then contacted with a detection probe comprising a nanoparticle-oligonucleotide conjugate such that the detection probe hybridizes to the target sequence component of the first hybridization complex. See Instant Specification, page 36, lines 19-31. In some embodiments, the instant specification recites, the detection probe can have a sequence complementary to a second domain of the target sequence (i.e., a part of the target sequence that is different than the domain to which the capture probe is complementary). See Instant Specification, page 37, lines 1-5; and page 11, line 32 to page 12, line 2. Alternatively, the detection probe can bind to the same domain as the capture probe, forming a triplex. See Instant Specification, page 12, lines 2-3. Thus, applicants respectfully submit that hybridization can take place in claim 1 between the capture probe and the target sequence. The use of the detection probe comprising an oligonucleotide as recited in Claim 14, refers to an embodiment wherein a further hybridization reaction takes place in addition to that between the capture probe and the target sequence.

Applicants respectfully submit that claim 16 refers to an embodiment such as illustrated in Figure 17B, which shows "a presently-described method of incorporating

one partner of a ligand-binding pair into a target nucleic acid," and wherein the ligand-binding partner can be used to bind a nanoparticle attached to the other member of the ligand-binding pair. See Instant Specification, page 7, lines 26-30. Thus, applicants submit that claim 16 refers to an embodiment wherein hybridization between a capture probe and a target sequence can take place as shown in the figure on the left-hand side of Figure 17B and is followed by a further reaction, one between a ligand-binding partner on the target sequence and a ligand-binding partner on a detection probe, wherein the detection probe comprises a ligand-binding partner and a nanoparticle as shown in the figure on the right-hand side of Figure 17B. Detection probes comprising a ligand-binding partner and a nanoparticle are described in the instant specification at page 35, lines 20-24.

Applicants respectfully submit that a single working example in the specification "is enough to preclude a rejection that nothing is enabled, since at least that embodiment would be enabled." See MPEP § 2164.02. Applicants respectfully submit that, as conceded by the Patent Office (see Office Action, page 5), the instant specification provides 5 working examples. In particular, Example 1 describes the use of 18 nucleotide long probe and target sequences attached to an indium tin oxide (ITO) substrate (i.e., solid surface) and 10 nm gold nanoparticles. See Instant Specification, page 58, lines 18-20. Example 4 describes the use of a glass substrate. See Instant Specification, page 61, lines 3-33. Example 3 describes 10 nm diameter gold nanoparticles illuminated by light at a wavelength of 532 nm associated with an ITO substrate surface (see Instant Specification, page 60, lines 3-8) and the detection of gold nanoparticles on a glass substrate surface (see Instant Specification, page 60, lines 21-23). Example 5 describes that the detection limit for hybridization complexes is 10 fM. See Instant Specification, page 62, lines 15-17. See, also, Instant Specification, Figure 16, which shows temperature changes observed in the presence of between 10 fM and 1000 pM DNA-gold nanoparticle conjugate.

With regard to the art cited in the Office Action, applicants respectfully submit that, in general, post-filing date references should not be used to demonstrate that

the patent is non-enabling. See MPEP § 2164.05(a), emphasis added. However, applicants appreciate that if such references indicate that one of skill in the art believes that an invention is not possible years after the filing date, the references can be used as evidence that the claimed subject matter is not possible at the time of filing. Id., citing *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ 1510, 1513-14 (Fed. Cir. 1993).

In this regard, applicants respectfully submit none of the references cited by the Office Action suggest that the detection of hybridization based on a change in temperature of a solid substrate following irradiation of a nanoparticle is impossible. Rather, these references appear to describe issues relating to errors that can occur in hybridization reactions generally. Even in this respect, applicants note that one of the post-filing references cited, Barany et al., (i.e., U.S. Patent Application Publication No. 2007/0042419) specifically recites that "a variety of DNA hybridization techniques are available for detecting the presence of one or more selected polynucleotide sequences in a sample containing a large number of sequence regions." Applicants also respectfully submit that the instant specification does appear to touch on several of the issues described by Carrico (i.e., U.S. Patent No. 5,200,313) in the section describing hybridization reactions. See Instant Specification, page 35, line 27 to page 39, line 16. In particular, the instant application provides specific hybridization conditions of varying stringency for varying sequence lengths and recites

> the temperature and ionic strength of a desired stringency are understood to be applicable to particular lengths of nucleic acid sequences, to the base content of the sequences, and to the presence of other compounds such as formamide in the hybridization mixture.

See Instant Specification, page 38, lines 1-4, emphasis added.

The instant specification further recites that conditions can be rendered more stringent by adding formamide (see Instant Specification, page 39, lines 12-13) and that hybridization at high temperature and/or low ionic strength relate to high stringency conditions. See Instant Specification, page 37, line 33 to page 38, line 1. Further, the instant specification describes that the use of two non-overlapping, non-complementary probes (i.e., a sandwich assay using a capture probe and a detection

probe comprising an oligonucleotide) can reduce the risk of "background noise" being interpreted as a false positive reading. See Instant Specification, page 21, line 25 to page 22, line 2. Sandwich assay embodiments can reduce the need to amplify a target sequence (e.g., to increase its concentration in a mixture), or, as noted hereinabove, the instant specification recites that in some cases, amplification can be desirable. See Instant Specification, page 18, lines 17-23. Moreover, the instant specification describes controls, such as comparing the detected signal of a hybridization reaction, for example, to a control wherein only non-target sequences are present. See Instant Specification, page 40, lines 10-12.

Particularly regarding the Patent Office's allegations concerning the possiblities for detecting false positives, applicants respectfully submit that the instant specification provides washing procedures to remove any unhybridized sequences (i.e., sequences not hybridized to a capture probe or to a hybridization complex comprising a capture probe, such as those the Patent Office describes which might form secondary structures. The instant specification notes "a high stringency wash followed by a low stringency wash to remove background probe signal." See Instant Specification, page 38, lines 27-28.

Thus, applicants respectfully submit that the instant specification provides a high level of guidance related to the presently claimed methods, including working examples. Accordingly, applicants respectfully request that the rejection of claims 1-43 under 35 U.S.C. § 112, first paragraph, for lack of enablement, be withdrawn. Applicants respectfully ask that claims 1-43 be allowed at this time.

IV. Response to the Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-43 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants view as the invention. In particular, the Patent Office alleges that claims 1-42 are indefinite with respect to what constitutes the metes and bounds of a "nanoparticle."

After careful consideration of the rejection and the Patent Office's comments, applicants respectfully traverse the rejection and offer the following remarks.

Initially, without acquiescing to the rejection or to the Patent Office's comments, applicants respectfully submit that, as noted hereinabove, claim 1 has been amended to recite that the nanoparticle comprises an approximately spherical metal-atom entity having a diameter of less than 1000 nanometers and exhibits one of surface plasmon resonance and an interband transition. Support for this amendment can be found in the instant specification at page 28, lines 31-33, which recites that a nanoparticle is an approximately spherical metal atom-comprising entity, and in the instant specification at page 29, lines 4-5, which recites that nanoparticles are generally less than 1000 nm in diameter. Support can also be found in the instant specification at page 29, lines 15-17, which recites that the nanoparticle can comprise a material that exhibits surface plasmon resonance, and in the instant specification at page 29, lines 22-23, which recites that the nanoparticle material can exhibit interband transitions. Further support can be found in the instant specification at page 11, lines 29-31, which recites that the nanoparticle "absorbs light at one or more particular frequencies (e.g. exhibits surface plasmon resonance or integrand transition)".

Accordingly, applicants submit that the metes and bounds of the term "nanoparticle" in claim 1 are clear. As claims 2-43 each ultimately depend from claim 1, claims 2-43 contain each and every element of claim 1. Accordingly applicants respectfully submit that the metes and bounds of the term "nanoparticle" in claims 2-43 is clear. Applicants respectfully request the withdrawal of the rejection of claims 1-43 under 35 U.S.C. § 112, second paragraph, and ask that claims 1-43 be allowed at this time.

V. New Claims

New claims 44-45 have been added.

New claim 44 is directed to a method of detecting a target nucleic acid sequence comprising providing an at least 10 fM concentration of a hybridization

complex comprising (a) a capture probe attached to a solid surface and (b) a target nucleic acid sequence hybridized to the capture probe, wherein the target nucleic acid sequence comprises a nanoparticle, wherein the nanoparticle comprises a metal or metal oxide that exhibits surface plasmon resonance, is approximately spherical, has a diameter of less than 1000 nanometers, and wherein the solid surface comprises a material different than the nanoparticle, and the capture probe comprises at least one oligonucleotide sequence that specifically hybridizes to the target sequence under stringent hybridization conditions. The method further comprises exposing the solid surface to light at a wavelength that matches the surface plasmon resonance of the nanoparticle and is not absorbed by the solid surface, and detecting a temperature of the solid surface, whereby detection of an increased temperature relative to a temperature of the solid surface that would be detected in the absence of the complex indicates the presence or amount of target nucleic acid sequence hybridized to the solid surface.

Support for new claim 44 can be found in claim 1 as originally filed. Support for providing a 10 fM concentration of a hybridization complex can be found in the instant specification at page 62, lines 15-17. Support for the nanoparticle comprising a metal or metal oxide can be found in the instant specification at page 30, lines 4-5. Support that the nanoparticle exhibits surface plasmon resonance can be found in the instant specification, for example, at page 29, lines 15-16. Support for the nanoparticle being approximately spherical and having a diameter of less than 1000 nm can found in the instant specification at page 28, line 32, and page 29, lines 4-5. Support for the solid surface being a material that is different than the material of the nanoparticle can be found in the instant specification at page 22, lines 15-17. Support of the capture probe comprising an oligonucleotide sequence that specifically hybridizes to the target under stringent conditions can be found in the instant specification at page 21, lines 15-18. Support for the light having a wavelength that matches the surface plasmon resonance of the nanoparticle can be found in the instant specification at page 41, lines 5-7. Support for the light being of

a wavelength not significantly absorbed by the solid support can be found in the instant specification at page 22, lines 13-15.

New claim 45 is directed to a method of detecting a target nucleic acid sequence comprising providing an at least 10 fM concentration of a hybridization complex comprising (a) a capture probe that is attached to a solid surface and (b) a target nucleic acid sequence that is hybridized to the capture probe, wherein the target nucleic acid sequence additionally comprises at least one approximately spherical gold nanoparticle having a diameter of between 5 and 200 nm attached to the target nucleic acid sequence. The method of claim 45 also comprises exposing the solid surface to light at a wavelength between about 510 nm and about 560 nm, and detecting a temperature of the solid surface, whereby detection of an increased temperature relative to a temperature of the solid surface that would be detected in the absence of said complex indicates the presence or amount of target nucleic acid sequence hybridized to the solid surface. New claim 45 further recites that providing a hybridization complex comprises: providing a capture probe comprising a 5 to 50 nucleotide sequence that is complementary to the target nucleic acid sequence; further wherein the capture probe is attached to a solid surface selected from glass and indium tin oxide (ITO); providing a target nucleic acid sequence comprising a nucleotide sequence of between 10 and 300 nucleotides; incubating the target nucleic acid sequence with the capture probe at a sodium ion concentration of less than 1.0 M, a pH of between 7.0 and 8.3, and at a temperature of at least 30°C; and removing any unhybridized target nucleic acid sequence.

Support for new claim 45 can be found in claim 1 as originally filed. Support for providing at least 10 fM hybridization complex can be found in the instant specification at page 62, lines 15-17. Support for the nanoparticle comprising gold can be found in the instant specification at page 30, line 13. Support for the nanoparticle being approximately spherical can be found in the instant specification at page 28, line 32. Support for the nanoparticle having a diameter of between 5 and 200 nm can be found in the instant specification at page 29, lines 9-10. Support for the solid surface comprising indium tin oxide (ITO) can be found in the instant

specification at page 10, lines 8-11. Support for the solid surface comprising glass can be found in the instant specification at page 22, line 23. Support for the exposing the solid surface to light at between 510 nm and about 560 nm can be found in the instant specification at page 41, line 21. Support for the capture probe comprising between 5 and 50 nucleotides complementary to a domain of the target sequence can be found in the instant specification at page 21, lines 21-22. Support for the target sequence comprising a nucleotide sequence of between 10 and 300 nucleotides can be found in the instant specification at page 16, lines 13-20. Support for the incubation conditions recited in new claim 45 can be found in the instant specification at page 39, lines 1-4. Support for removing unhybridized target sequence can be found in the instant specification at page 36, lines 9-11.

Applicants respectfully submit that new claims 44-45 are in condition for allowance and ask for a Notice of Allowance to that effect.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any additional fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: August 31, 2007 By: _____

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